

**REMARKS**

Claims 73-86 are under examination.

As per 37 C.F.R. § 1.121(c)(1), amendments are presented in clean form in the body of this filing and in marked-up form in the attached Appendix.

**I. The Rejections Of The Claims For Non-Statutory Double Patenting**

The claims stand provisionally rejected for non-statutory double patenting on two grounds.

*1. The '105 Application*

Claims 73-86 stand provisionally rejected for non-statutory double patenting over claims 1-177 of U.S. Patent Application No. 09/159,105 (“the ‘105 application”) in view of MedLine 98242495 (“Feghali”).

The Office has maintained this rejection “for the reasons of record” (Office Action, page 2, paragraph #2). The non-final Office Action dated 19-Sep-01 (“the non-final Action”) asserted that claims 1-177 of the ‘105 application recite treating a disorder generically embraced by the present claims and that the disclosed compounds encompass those recited in the present claims (September 19 Office Action, page 2, paragraph #2).

Applicants respectfully traverse.

According to the M.P.E.P., a provisional double patenting rejection may be due between “two copending applications filed by the same inventive entity, or by different inventive entities having a common inventor, and/or by a common assignee.” M.P.E.P. § 804.I.B., page 800-19 (8<sup>th</sup> Ed., August 2001).

The present application is assigned to "GPI NIL Holdings, Inc." which is now entirely owned by Guilford Pharmaceuticals Inc. The '105 application is not assigned to GPI NIL Holdings, Inc. or any company related to Guilford Pharmaceuticals Inc. Applicants have therefore been unable to obtain a copy of the '105 application. However, WO 99/14,998 (of record in this case in Form PTO-892 of Paper No. 17) claims priority to and therefore likely corresponds to the '105 application. WO 99/14,998 has no common inventors with the '105 application. The '105 application is therefore not an application "filed by the same inventive entity, or by different inventive entities having a common inventor, and/or by a common assignee" and cannot support a provisional double patenting rejection. The rejection should thus be withdrawn.

2. *The '187, '797, '423, and '607 Patents*

Claims 73-86 stand provisionally rejected for non-statutory double patenting over claims 9-12 of U.S. Patent No. 5,801,187 ("the '187 patent"), claims 15-16 of No. 5,846,797 ("the '797 patent"), claims 1-37 of No. 6,218,423 ("the '423 patent"), and claims 17-20 of No. 6,274,607 ("the '607 patent") in view of claims 1-177 of the '105 application.

The Office has maintained this rejection "for the reasons of record" (Office Action, page 2, paragraph #3). The non-final Action asserted that the claims include both carboxylic acid and carboxylate bioisosteres, and that the latter are prima facie obvious over the carboxylate disclosed in the '187 patent (non-final Action, page 3, paragraph #5).

This ground of rejection would be obviated by the proposed amendment. The claims as amended do not recite carboxylate ester bioisosteres.

## **II. The Rejection Of Claims 73-86 Under 35 U.S.C. § 103(a)**

Claims 73-86 stand rejected under 35 U.S.C. § 103(a) over the '187 patent in view of F.D. King, Med. Chem.: Principle & Practice (1994) 206 ("King") or G.P. Patani et al., Chem. Rev., 1996, Vol. 96, p. 3147 ("Patani"). The Office considers that it would have been obvious to replace the carboxylate ester groups of the '187 patent with carboxylate ester bioisosteres (Office Action, page 3, paragraph #4).

This ground of rejection would be obviated by the proposed amendment. The claims as amended do not recite carboxylate ester bioisosteres.

## **III. The Rejection Of Claims 73-86 Under 35 U.S.C. § 112**

Claims 73-86 stand rejected under 35 U.S.C. § 112 as allegedly indefinite due to the terms "carboxylic acid" and "carboxylic acid isosteres" conflicting with carboxylate ester isostere Markush elements (Office Action, paragraph bridging pages 2-3). This ground of rejection would be obviated by the proposed amendment. The claims as amended do not recite carboxylate ester isosteres.

## **IV. CONCLUSION**


Applicants submit that the proposed amendments would place the pending claims in condition for allowance, would raise no new issues, and would not require further search. Applicants request that the Office exercise its discretion under Rule 116 to enter the amendments and allow the resulting claims. If the Office has questions, the Office is invited to call Applicants' Representative directly at (202) 974-6018.

Please charge or credit Deposit Account No. 12-2475 for all fees as needed.

Respectfully submitted,

LYON & LYON LLP

Dated: 1-Jul-2002

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**APPENDIX A:**

**MARKED-UP VERSION OF AMENDMENTS TO THE SPECIFICATION**

*Please replace the paragraph on page 1, lines 6-10, with the following:*

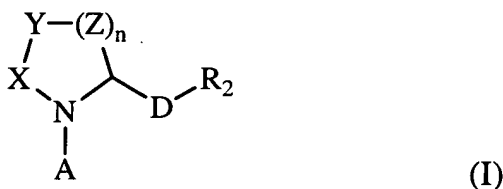
This application is a non-provisional of [continuation-in-part of] U.S. provisional [patent] application serial number 60/087,843 [to Hamilton et al., entitled "Carboxylic Acids and Carboxylic Acid Isosteres of Heterocyclic Ring Compounds Having Multiple Heteroatoms,"] filed June 3, 1998.

**APPENDIX B:**

**MARKED-UP VERSION OF AMENDED CLAIMS**

73. (Amended) A method of treating a neurological disorder in an animal, comprising:

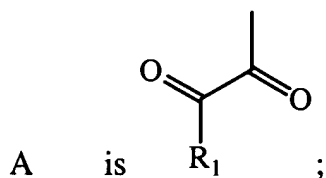
administering to the animal an effective amount of a compound to stimulate growth of damaged peripheral nerves or to promote neuronal regeneration, wherein the compound has the formula (I):



where

X, Y, and Z are independently selected from the group consisting of C, O, S, or N, provided that X, Y, and Z are not all C;

n is 1;

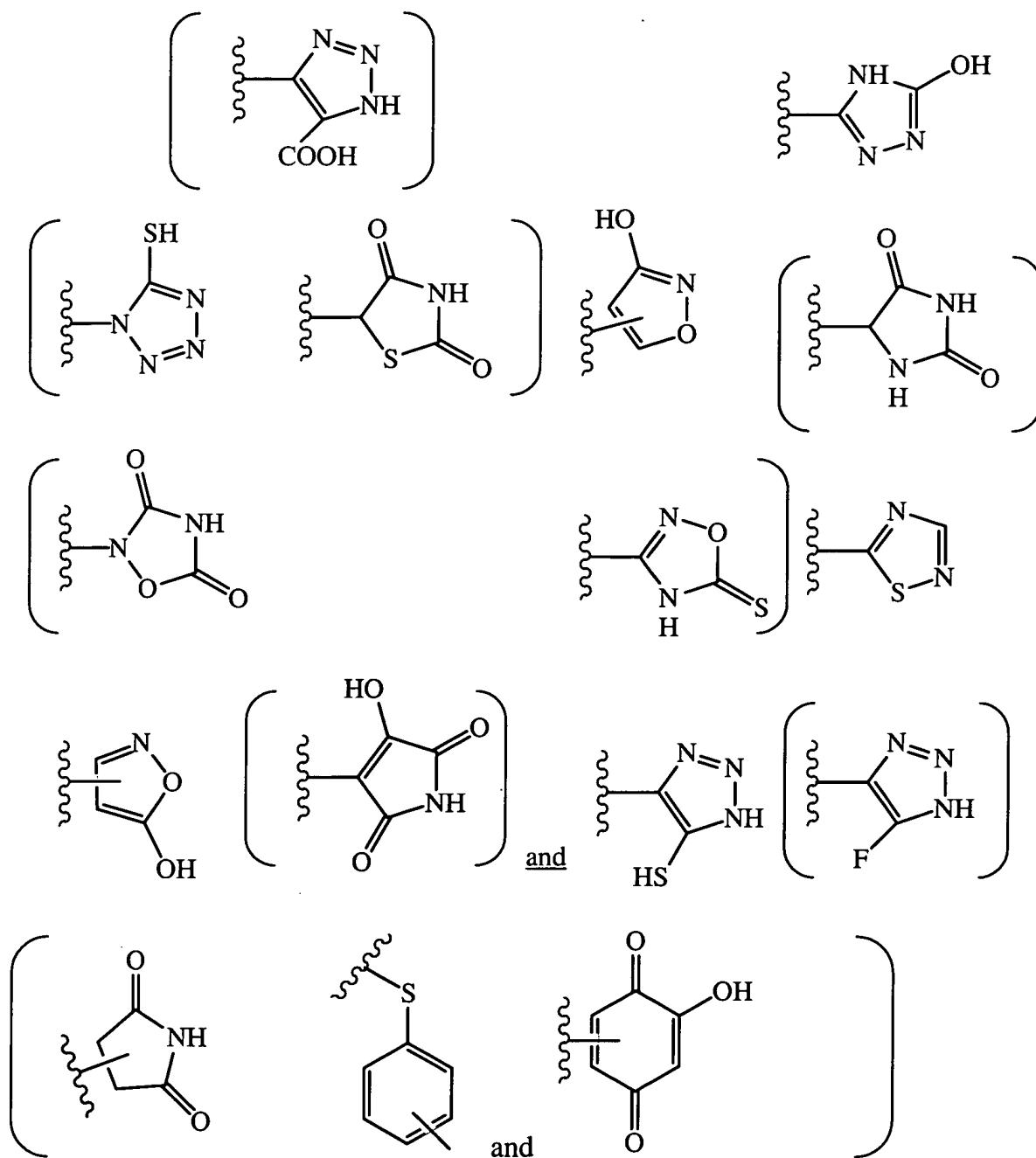


R<sub>1</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, and heterocycle;

D is selected from the group consisting of a bond, C<sub>1</sub>-C<sub>10</sub> straight or branched chain alkylene, ethylene (-C=C-), and butylene;

R<sub>2</sub> is a carboxylic acid or a carboxylic acid isostere selected from the group consisting

of:

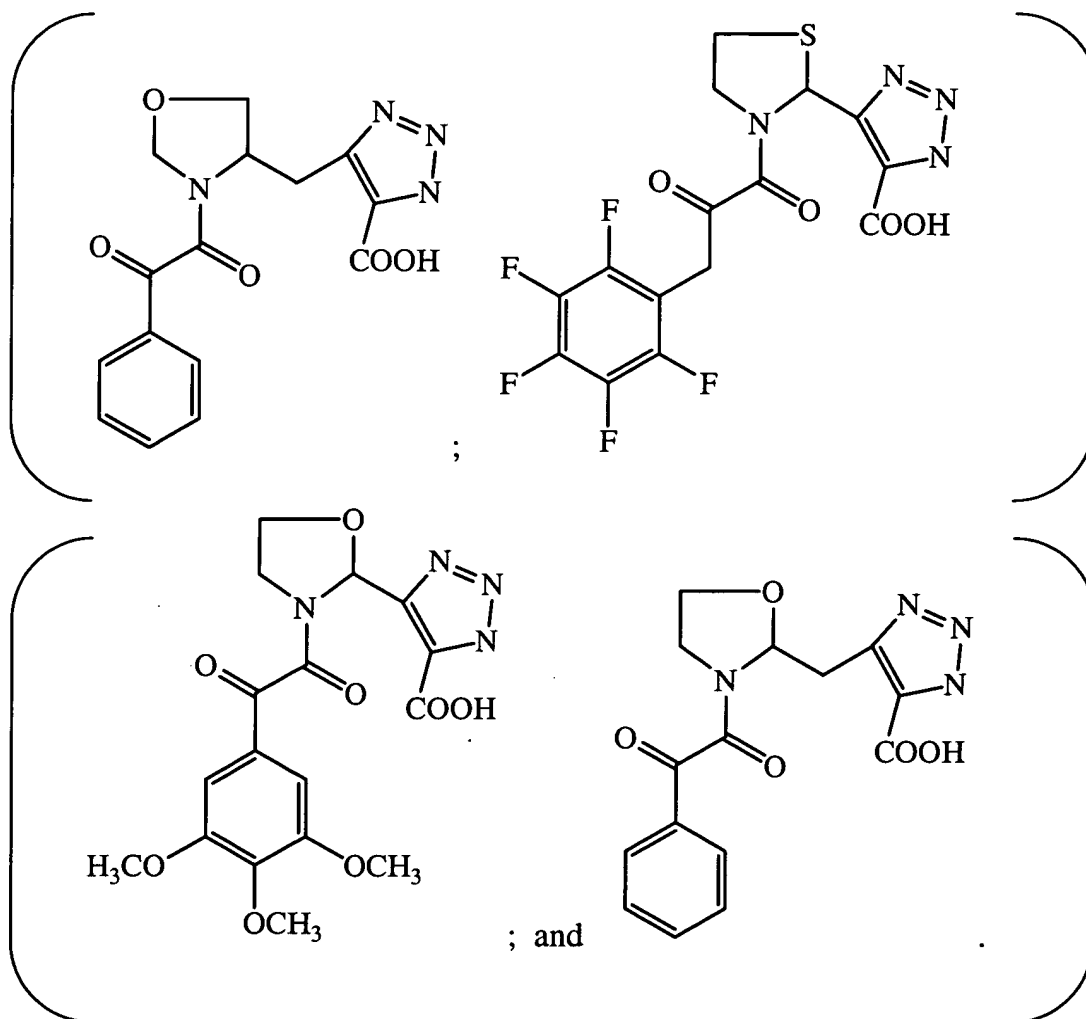


or a pharmaceutically acceptable salt, or solvate thereof.

the compound is selected from the group consisting of:

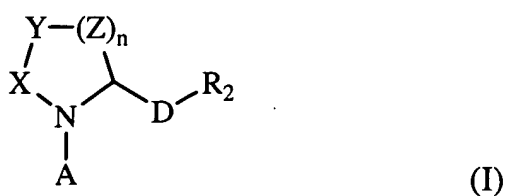






80. (Amended) A method of treating a neurological disorder in an animal, comprising:

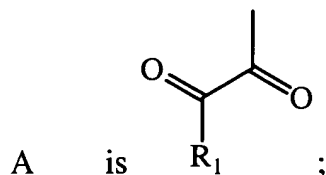
administering to the animal an effective amount of a compound to stimulate growth of damaged peripheral nerves or to promote neuronal regeneration, wherein the compound has the formula (I):



where

X, Y, and Z are independently selected from the group consisting of C, O, S, or N, provided that X, Y, and Z are not all C;

n is 1;



R<sub>1</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, and heterocycle;

D is selected from the group consisting of a bond, C<sub>1</sub>-C<sub>10</sub> straight or branched chain alkylene, ethylene (-C=C-), and butylene;

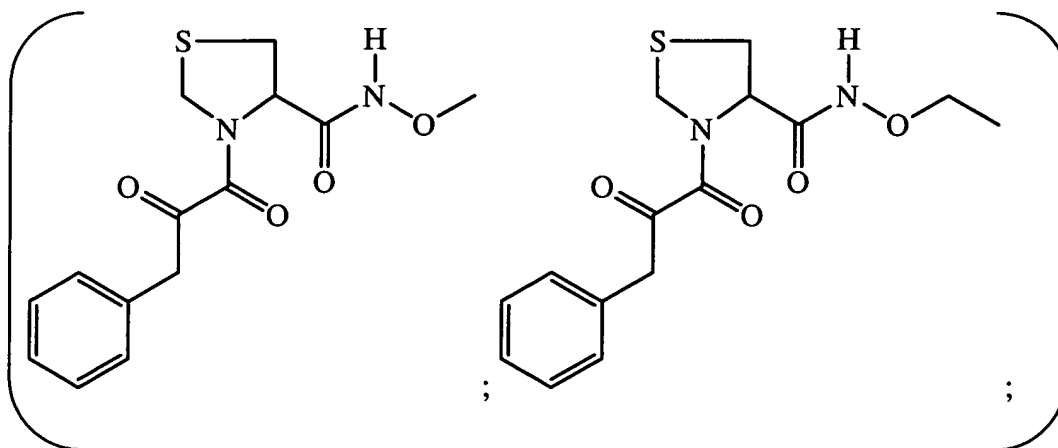
R<sub>2</sub> is a carboxylic acid or a carboxylic acid isostere selected from the group consisting of:

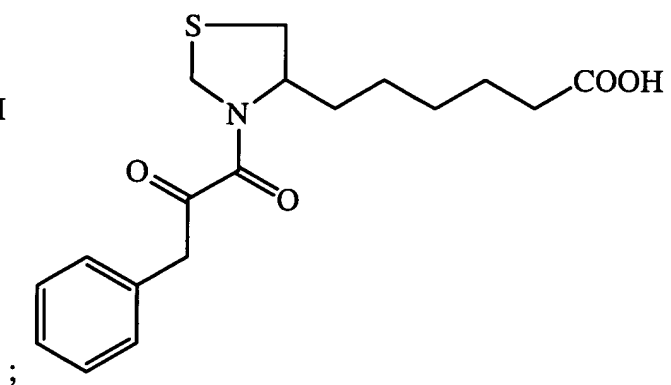
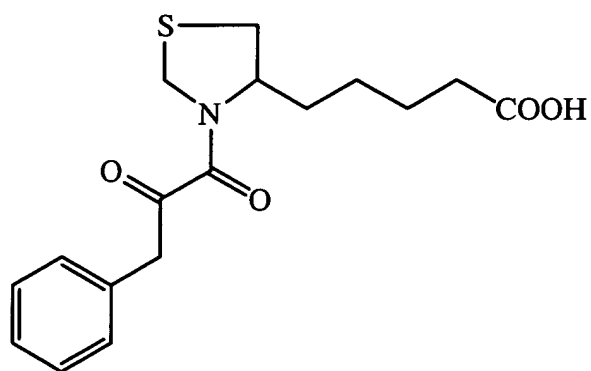
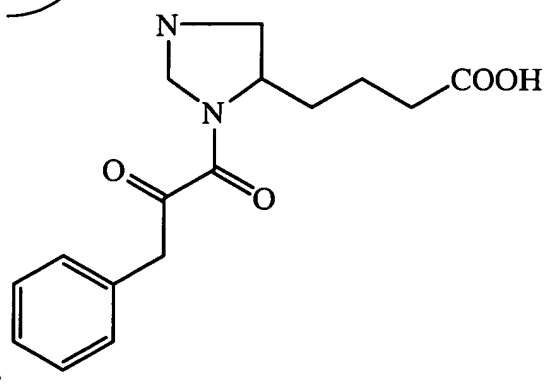
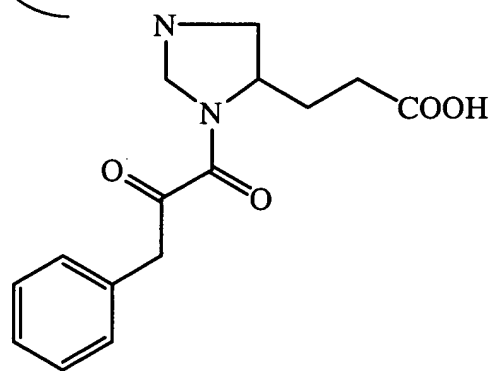
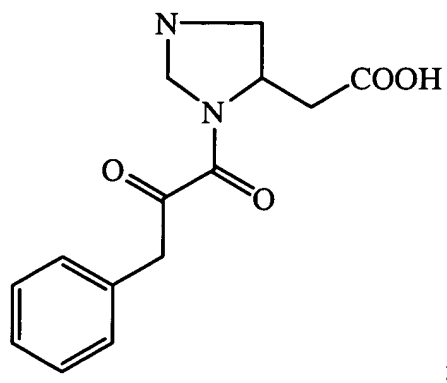
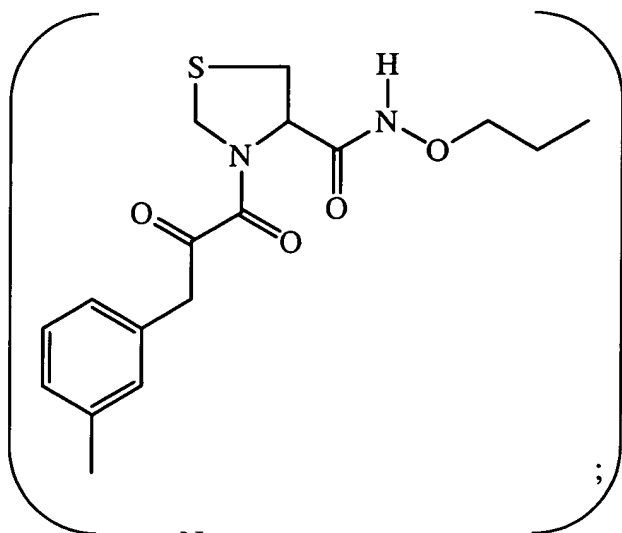
-COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sub>3</sub>, -PO<sub>2</sub>H, [-PO<sub>2</sub>(R<sub>3</sub>)<sub>2</sub>], -CN, [-PO<sub>3</sub>(R<sub>3</sub>)<sub>2</sub>], -PO(OH)(OR<sub>3</sub>), [-OR<sub>3</sub>, -SR<sub>3</sub>, -NHCOR<sub>3</sub>, -N(R<sub>3</sub>)<sub>2</sub>, -CON(R<sub>3</sub>)<sub>2</sub>, -CONH(O)R<sub>3</sub>,] -C(O)NHOH, [-CONHNHSO<sub>2</sub>R<sub>3</sub>, -COHNSO<sub>2</sub>R<sub>3</sub>, and -CONR<sub>3</sub>CN] -C(O)NHHSO<sub>2</sub>R<sub>3</sub>, and -CONHCN;

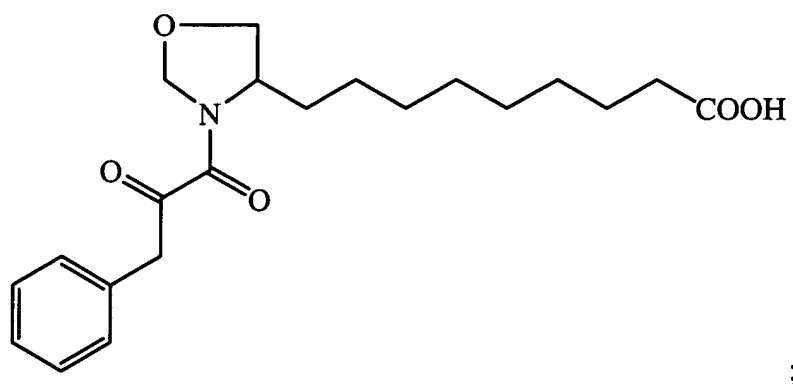
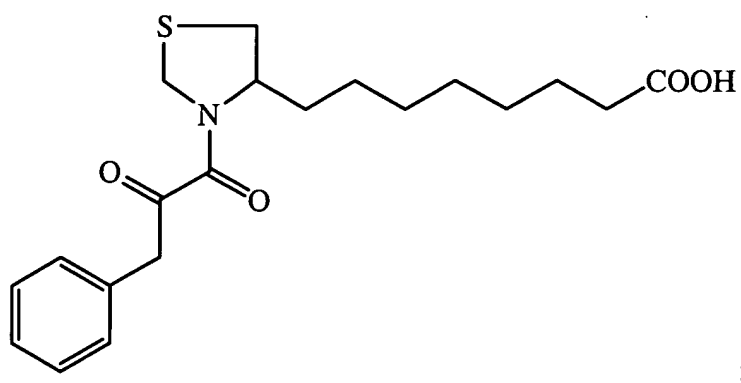
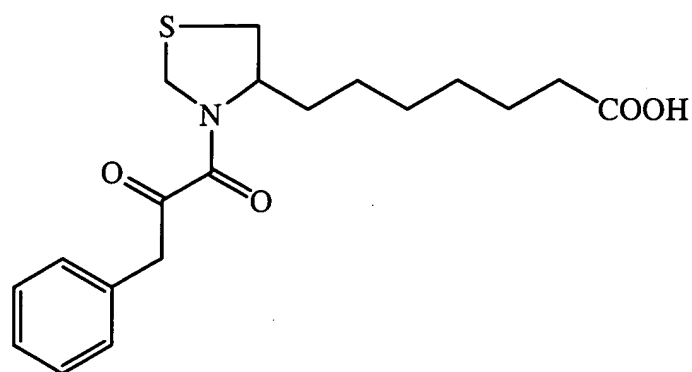
wherein said alkyl, alkenyl, alkylene, ethylene, butylene, aryl, heteroaryl, carbocycle, heterocycle, or carboxylic acid isostere is optionally substituted with one or more substituents selected from R<sub>3</sub>, where

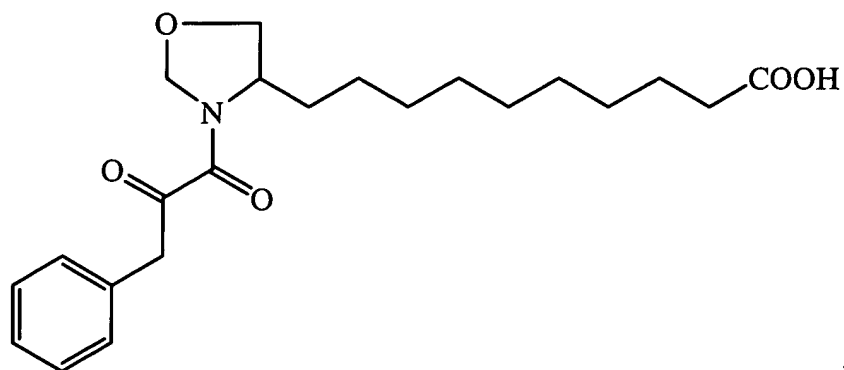
$R_3$  is selected from the group consisting of hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl,  $C_1$ - $C_6$  straight or branched chain alkyl,  $C_2$ - $C_6$  straight or branched chain alkenyl or alkynyl, aryl, heteroaryl, carbocycle, heterocycle, and  $CO_2R_4$  where  $R_4$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  straight or branched chain alkyl, and  $C_2$ - $C_9$  straight or branched chain alkenyl;  
or a pharmaceutically acceptable salt, or solvate thereof.

86. (Amended) The method of claim 80, wherein the compound is selected from the group consisting of:

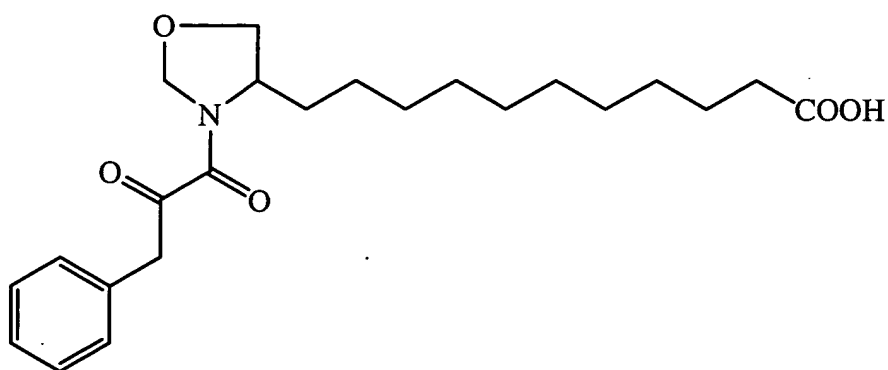




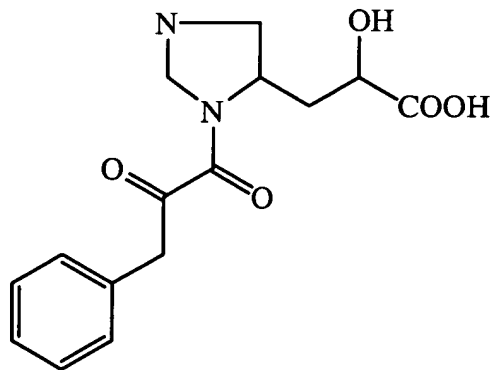
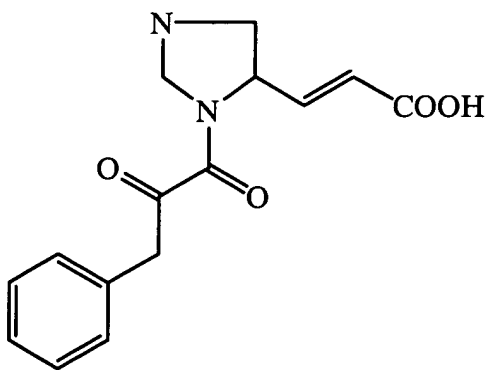




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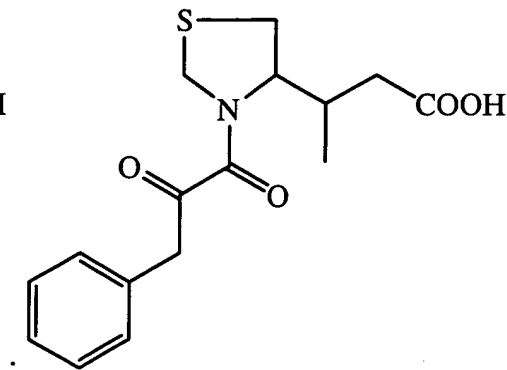
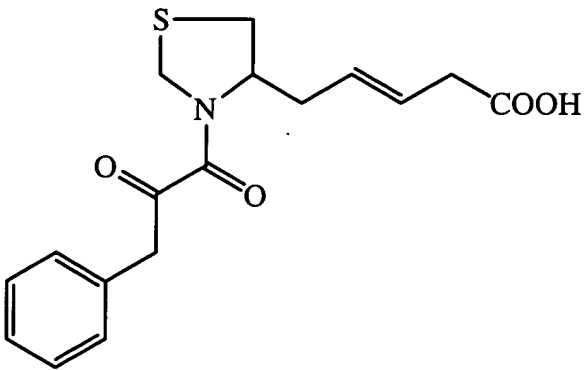


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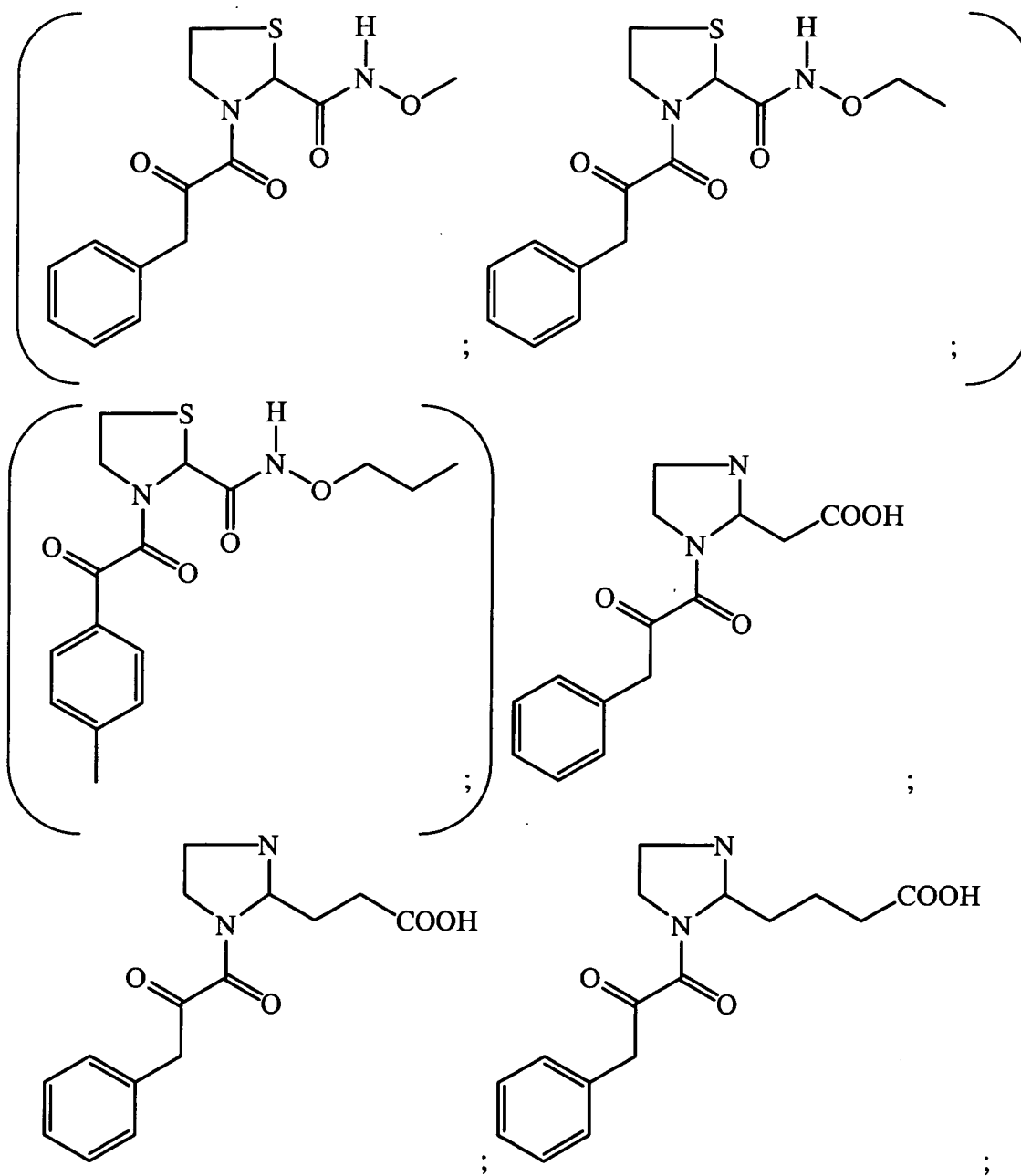
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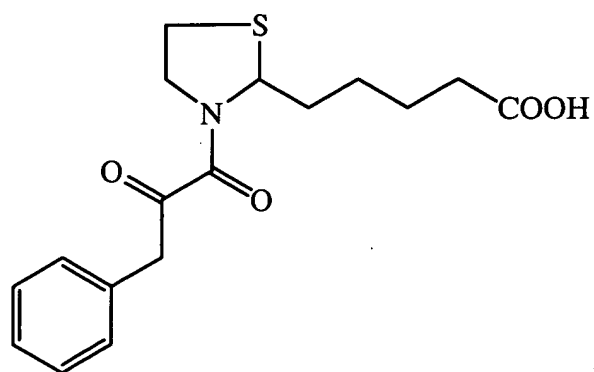
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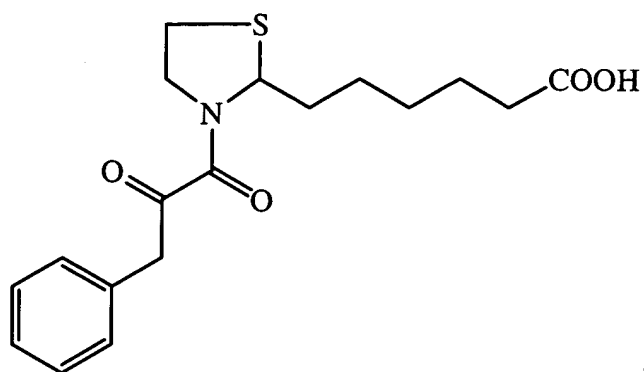
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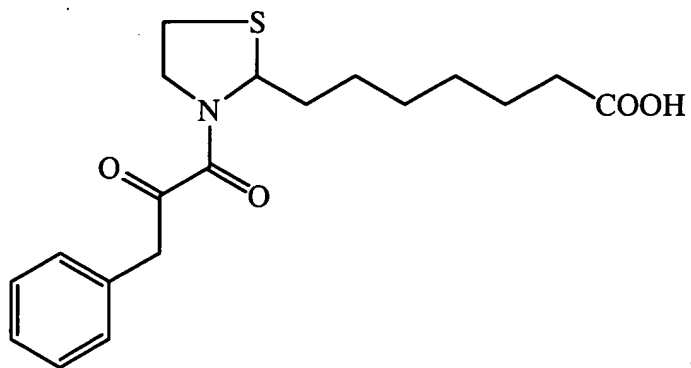




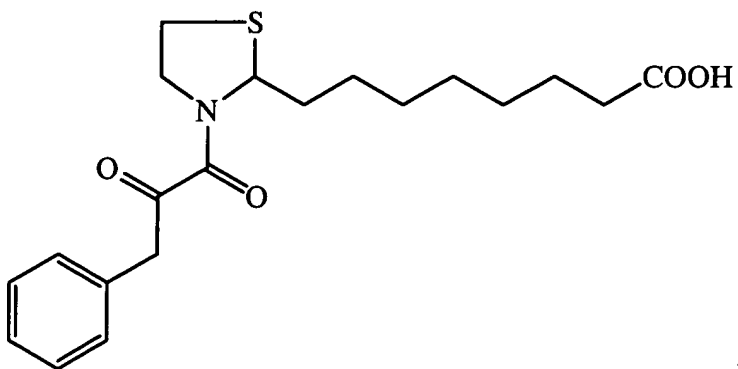
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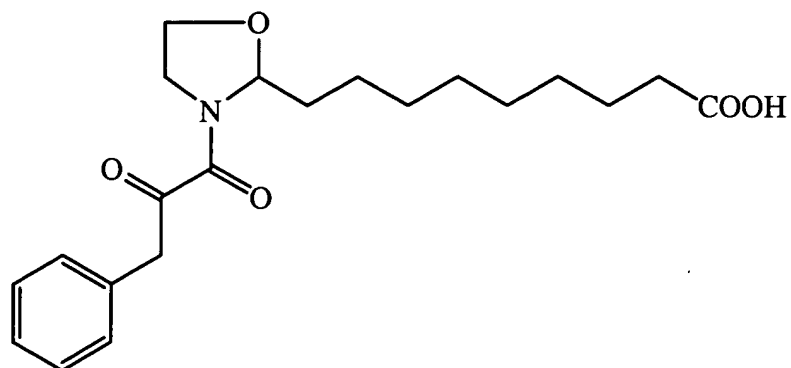


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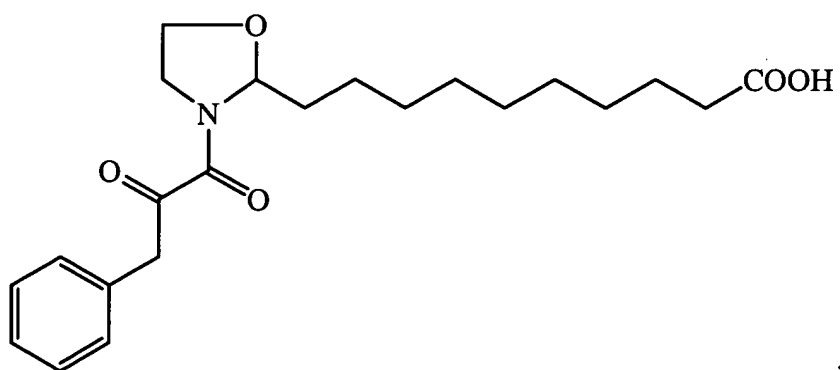


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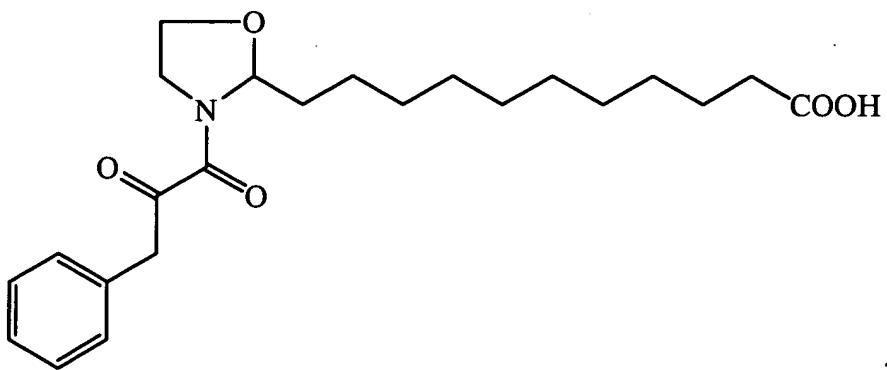




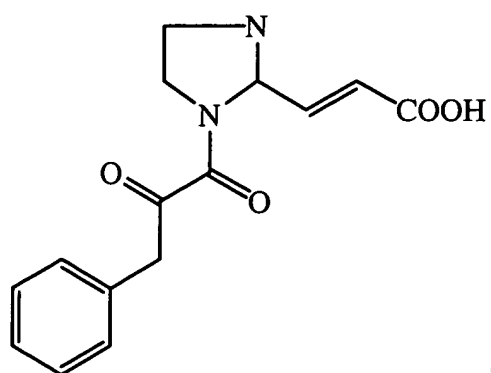
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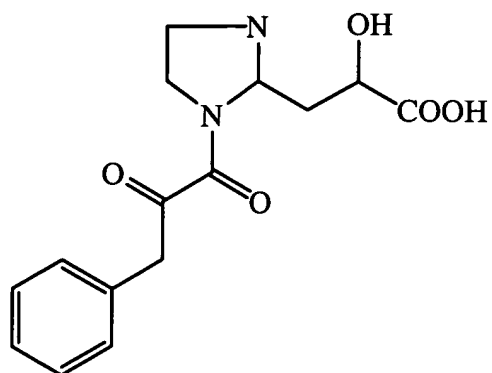
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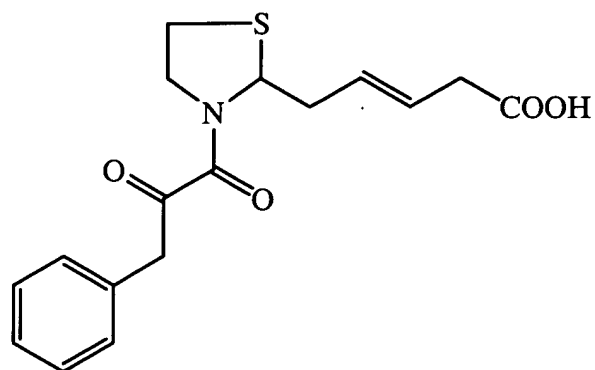
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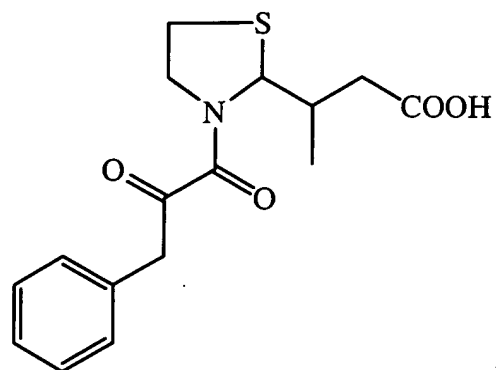
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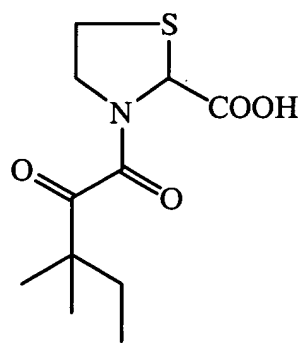
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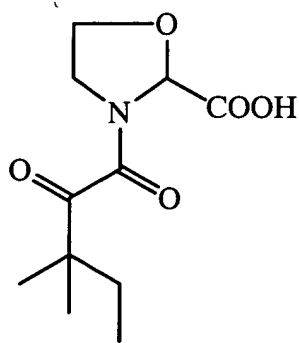
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